REMARKS

Claims 1, 2 and 4-60 and 70-75 presently appear in this case. Claims 35-69 (of which claims 61-69 have now been cancelled without prejudice to continuation of prosecution thereof in a divisional application) have been withdrawn from consideration. No claims have been allowed. The official action of September 7, 2007, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a cell line (and to a composition and kit containing this cell line and to methods of using this cell line), which is essentially a "one-time use" commercial cell line with a shelf life suitable for its intended use in an assay, after which (no more than thirty days) the cell losses signal transduction activity and undergoes cellular death.

The interview, graciously granted, among Examiners Mitchell and Sullivan, applicant's attorneys, Allen Yun and Roger Browdy, and the inventor, Dr. Michael Tovey, which interview was conducted on September 10, 2007, is hereby gratefully acknowledged. In this interview, the proposed changes to the claims as presented herein were discussed and the examiners agreed that this amendment would likely overcome the prior art rejections currently of record. The written description and enablement rejections were also discussed. Applicant stated that a declaration would be introduced presenting multiple examples of cell lines produced in an attempt to establish that it would not involve undue experimentation to practice the present invention as broadly claimed and that applicants were in possession of the full breadth of the present claims. The arguments presented at the interview will be repeated in the discussion of the rejections hereinbelow.

Claims 1-34 and 70-75 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The examiner states that this is in the nature of a new matter rejection. The examiner states that claims 1 and 2 have been amended to recite the additional limitation that the cell line "will lose said signal transduction activity and undergo cellular death in no more than about thirty days at a temperature above freezing," and that claims 70 and 71 add similar limitations. The examiner objects to the fact that claims 1 and 2 do not recite that the cell lines have been treated in any manner that would convey the property of cellular death in no more than about thirty days. The examiner states that the specification does not disclose an untreated cell line with this property. Therefore, the examiner considers that amended claims 1, 2 and new claim 70-71 constitute impermissible new matter. This part of the rejection is respectfully traversed.

Claims 1 and 2 have now been amended to specify that the cell line has been treated with an anti-mitotic and pro-apoptotic agent so as to acquire the specified properties. Claim 3, which previously recited this feature, has now been deleted. As indicated in claims 7-9, the agent with which the cell line has been treated may be a chemical or it may be γ-irradiation. Accordingly, this part of the rejection has now been obviated.

The written description rejection further states that the present claims have not established a structure-function relationship between the anti-mitotic and pro-apoptotic agent and maintenance of the signal transduction activity for a particular time and cell death after a particular time period. The examiner states that the genus of possible cell lines is very broad, as is the class of cell surface receptors encompassed by the claims. The examiner states that the claims cover a broad range of transcriptional control elements, but only a few have been disclosed. The examiner states that there is not a structural and functional basis provided by the prior art or the specification for one of ordinary skill in the art to envision all cell lines with the claimed characteristics, and thus one of ordinary skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support them. This part of the rejection is respectfully traversed.

The present invention presents nothing new with respect to reporter gene assays. Reporter gene assays are well known in the prior art, as can be seen, for example, by the prior art cited by the examiner, and particularly the

Harpold patents. The present invention is directed to an improvement of the recombinant cell lines that are conventionally used in such assays, by which such cell lines may become more commercially viable. By means of the present invention, any known reporter gene cell line can be treated in such a manner that it can only be used once. The signal transduction activity will be retained for at least an hour, but after no more than about thirty days, the cell line will lose its signal transduction activity and will die. Thus, one of ordinary skill in the art would understand that applicant was in possession of the full breadth of the claimed reporter gene assay cell lines that are the starting point of the present invention and which are treated in order to produce the claimed improved cell lines that can only be used once.

As to the claimed treatment with an anti-mitotic and pro-apoptotic agent that can be used in order to cause the cell line to acquire the property that it will maintain the signal transduction activity for at least one hour, but will lose the signal transduction activity and undergo cellular cell death in no more than about thirty days at a temperature above freezing, this is adequately described in the specification, such that one of ordinary skill in the art would understand that applicant was in possession thereof. γ-irradiation is anti-mitotic and pro-apoptotic and this is fully explained in the present specification at pages 35-37. Many cancer chemotherapy drugs, such as vinblastin, 5FU or cisplatin, are known to be anti-mitotic and pro-apoptotic. As several specific examples of anti-mitotic and pro-apoptotic agents are disclosed in the present specification, this is a sufficient number to reasonably establish that applicant was in possession of the full scope of the claims. Those of ordinary skill in art could readily determine what other agents may be anti-mitotic and pro-apoptotic and, without undue experimentation (as will be discussed below), determine the concentrations and contact times that will cause the cell lines treated therewith to fall within the parameters of the present claims.

There is no reason to believe that any other cell line cannot be treated as disclosed in the present specification so as to attain the claimed characteristics. Indeed, the experiments discussed below with respect to the enablement rejection establishes this.

For all of these reasons, one of ordinary skill in the art would conclude that applicant was in possession of the claimed genus. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 1-34 and 70-75 have been rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a promonocytic cell line that has been treated with an anti-mitotic and pro-apoptotic agent, does not reasonably provide enablement for a cell line of any other type of cell and therefore the specification does not enable a person of ordinary skill in the art to make the invention commensurate in scope with these claims. The examiner then examines the *Wands* factors to determine whether or not undue experimentation would be required to practice the present invention. The examiner concludes that the skilled artisan would have to practice undue and excessive experimentation in order to practice the claimed invention. This rejection is respectfully traversed.

As discussed above, the starting point of the present invention is cells that have been transformed with a reporter gene construct comprising a nucleotide sequence encoding a reporter gene product operatively linked to one or more transcriptional control elements that are regulated by the signal transduction activity of a cell surface protein in response to an extracellular signal. Such cell lines are well known in the art, and such cell lines, *per se*, do not form part of applicant’s invention. The present invention relates to an improvement in such known cell lines by which they may acquire a “one-time use” characteristic. Thus, it would not entail undue experimentation to obtain cell lines within the scope of the starting materials used in the present invention, as such are well known, as is evidenced, for example, by the art cited by the examiner, particularly including the Harpold patents.

The improvement of the present invention is the treatment of such cell lines with an anti-mitotic and pro-apoptotic agent so that such cell lines may acquire the property of maintaining the signal transduction activity for at least about one hour while losing such signal transduction activity and undergoing cellular death in no more than about thirty days at a temperature above freezing. Part of the present enablement rejection is that one of ordinary skill in the art would need to do undue experimentation to determine appropriate amounts of anti-mitotic and pro-apoptotic agent that would permit the invention to work with differing kinds of cell lines, with differing cell cycles, etc.

In order to show that undue experimentation would not be involved in practicing the present invention, attached hereto is a declaration of Dr. Michael Tovey detailing experimentation that has been conducted following the guidelines of the present specification. The experiments presented in Dr. Tovey's declaration demonstrate that a variety of human cell types (promonocytic, myeloid, T-cell lymphoma, breast adenocarcinoma) and non-human cells (mouse lymphoma), all treated with the same concentration of vinblastin and the same conditions before being cryopreserved in ampoules/vials as taught in the above-identified application on pages 47 and 48, are all capable of maintaining signal transduction activity for at least 24 hours after being thawed, as well as undergoing cellular death in no more than thirty days at a temperature above freezing. Thus, the additional experiments reported in the Tovey declaration use conditions that were optimized for PIL5 cells, so as to obtain induction of apoptosis in 100% of the cell population while maintaining fully functional signal transduction for at least 24 hours after thawing. When these same optimal conditions were applied to the other cell lines/types, without further experimentation, they were all found to have the properties required by the present claims. Apoptosis was induced in 100% of each of the cell populations within thirty days, and yet fully functional signal transduction was maintained for at least 24 hours after thawing.

Accordingly, the variability indicated by the examiner does not appear to be a significant factor. Operable conditions can be determined by one of ordinary skill in the art without undue experimentation. Indeed, no experimentation is needed as in every cell type tested the experimental conditions provided in the present specification were operable to obtain the properties required by the present claims. If a cell type is found that does not maintain signal transduction activity for 24 hours after thawing or which does not undergo apoptosis within thirty days, then only minimal experimentation would be necessary to change the concentration or time of treatment with the anti-mitotic and pro-apoptotic agent and then again test the cell line to find the conditions that will cause the cell line to have the properties that fall within those required by the claims. Once one of ordinary skill in the art understands the concept of the present invention, it can readily be practiced for any given cell line with only minimal, if any, experimentation. Certainly, the amount of experimentation necessary is less than that which was found permissible in the *Wands* case cited by the examiner, which involved screening of multitudes of hybridomas for those producing the desired antibodies.

Accordingly, as the declaration shows that the present invention is indeed operable for many different types of cells lines, as predicted in the present specification, and as operable conditions have been found for each of the tested diverse cell lines without undue experimentation, indeed without any additional experimentation at all, and for the other reasons discussed herein, the full scope of the present claims should be considered to comply with the enablement requirement of the first paragraph of 35 U.S.C. 112. Reconsideration and withdrawal of this rejection is therefore respectfully urged.

Selected ones of the present claims have been subject to numerous prior art rejections. However, claims 3 and 34 have not been rejected over any of the prior art of record or any combination thereof. As the subject matter of claim 3 has now been inserted into claim 1 and all of the present claims, other than claim 34, are dependent from claim 1, none of the present prior art rejections remain applicable. Accordingly, all of the present claims are now free of the prior art. Reconsideration and withdrawal of the all of the prior art rejections are therefore respectfully urged.

Submitted herewith is an IDS citing U.S. patent 7,045,281 to Livelli et al, which the examiner may find to be pertinent to the present claims. In order to obviate any prospective rejection based on this reference, attached hereto is a Declaration under 37. CFR 1.131 by the present inventors and a supporting declaration of Allen Yun. These declarations establish conception prior to the September 20, 2002, filing date of Livelli and diligence in preparing and filing the provisional patent application that was filed on October 4, 2002, from which the present application claims benefit under 35 USC 119(e). This attorney/agent diligence extended from prior to September 20, 2002, until the filing of the provisional application on October 4, 2002. Accordingly, Livelli has been antedated and is not available as a reference in this case.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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